

Amendments to the Specification:

Please replace the paragraphs at page 22, line 30 to page 23, line 6, with the following amended paragraphs:

Figures 5A-5N, are ~~Figure 5~~ is a schematic representation of the fourteen fragments (Fragments A-Fragment N) assembled to construct pXF8.61.

Figures 6A-6E, are ~~Figure 6~~ is a schematic representation of the assembly of pXF8.61.

Figures 7A-7C, Figure 7 depict[[s]] the nucleotide sequence and the corresponding amino acid sequence of the LE B-domain-deleted-Factor VIII (FVIII)insert contained in pAM1-1 (SEQ ID NO:1).

Figure 8 is a schematic representation of the fragments assembled to construct pXF8.186.

Figures 9A-9C, Figure 9 depict[[s]] the nucleotide sequence and the corresponding amino acid sequence of the 5Arg B-domain-deleted-FVIII insert (SEQ ID NO:2).

Please replace the paragraph at page 48, lines 4-16, with the following amended paragraph:

The fourteen gene fragments of the B-domain-deleted-FVIII optimized cDNA listed in Table 2 and shown in Figures 5A-5N ~~Figure 5~~ (Fragment A-Fragment N) were made as follows. 92 oligonucleotides were made by oligonucleotide synthesis on an ABI 391 synthesizer (Perkin Elmer). The 92 oligonucleotides are listed in Table 3. Figures 5A-5N ~~Figure 5~~ show[[s]] how these 92 oligonucleotides anneal to form the fourteen gene fragments of Table 2. For each strand of each gene fragment, the first oligonucleotide (i.e. the most 5') was manufactured with a 5'-hydroxyl terminus, and the subsequent oligonucleotides were manufactured as 5'-phosphorylated to allow the ligation of adjacent annealed oligonucleotides. For gene fragments A,B,C,F,G,J,K,L,M and N, six oligonucleotides were annealed, ligated, digested with EcoRI and HindIII and cloned into pUC18 digested with EcoRI and HindIII. For gene fragments D, E, H and I, eight oligonucleotides were annealed, ligated, digested with EcoRI and HindIII and cloned

into pUC18 digested with EcoRI and HindIII. This procedure generated fourteen different plasmids-- pAM1A through pAM1N.

Please replace the paragraph at page 53, line 2 to page 54, line 27, with the following amended paragraph:

As noted in Table 2 and shown in Figures 5A-5N ~~Figure 5~~, fragment D was constructed with a BamHI restriction site placed between the BglII site and the HindIII site at the 3' end of the fragment. Fragment I was constructed to carry the DNA from PmlI (2491) to BstEII (2661) followed immediately by the DNA from BstEII (2955) to KpnI (3170), so that the insertion of the BstEII fragment from pAMJ into the BstEII site of pAMI in the correct orientation will generate the desired sequences from 2491 to 3170. Plasmid pAM1B was digested with ApaI and HindIII and the insert was purified by agarose gel electrophoresis and inserted into plasmid pAM1A digested with ApaI and HindIII, generating plasmid pAM1AB. Plasmid pAM1D was digested with PmlI and HindIII and the insert was purified by agarose gel electrophoresis and inserted into plasmid pAM1AB digested with PmlI and HindIII, generating plasmid pAM1ABD. Plasmid pAM1C was digested with PmlI and the insert was purified by agarose gel electrophoresis and inserted into plasmid pAM1ABD digested with PmlI, generating plasmid pAM1ABCD, insert orientation was confirmed by the appearance of a diagnostic 111bp fragment when digested with MscI. Plasmid pAM1F was digested with BglII and HindIII and the insert was purified by agarose gel electrophoresis and inserted into plasmid pAM1E digested with BglII and HindIII, generating plasmid pAM1EF. Plasmid pAM1G was digested with KpnI and HindIII and the insert was purified by agarose gel electrophoresis and inserted into plasmid pAM1EF digested with KpnI and HindIII, generating plasmid pAM1EFG. Plasmid pAM1J was digested with BstEII and the insert was purified by agarose gel electrophoresis and inserted into plasmid pAM1I digested with BstEII, generating plasmid pAM1IJ; orientation was confirmed by the appearance of a diagnostic 465bp fragment when digested with EcoRI and EagI. Plasmid pAM1IJ was digested with PmlI and HindIII and the insert was purified by agarose gel electrophoresis and inserted into plasmid pAM1H digested with PmlI and HindIII, generating

plasmid pAM1HIJ. Plasmid pAM1M was digested with EcoRI and BstEII and the insert was purified by agarose gel electrophoresis and inserted into plasmid pAM1N digested with EcoRI and BstEII, generating plasmid pAM1MN. Plasmid pAM1L was digested with EcoRI and SmaI and the insert was purified by agarose gel electrophoresis and inserted into plasmid pAM1MN digested with EcoRI and EcoRV, generating plasmid pAM1LMN. Plasmid pAM1LMN was digested with ApaI and HindIII and the insert was purified by agarose gel electrophoresis and inserted into plasmid pAM1K digested with ApaI and HindIII, generating plasmid pAM1KLMN. Plasmid pAM1EFG was digested with BamHI and the insert was purified by agarose gel electrophoresis and inserted into plasmid pAM1ABCD digested with BamHI and BglII, generating plasmid pAM1ABCDEFG; orientation was confirmed by the appearance of a diagnostic 552bp fragment when digested with BglII and HindIII. Plasmid pAM1KLMN was digested with KpnI and HindIII and the insert was purified by agarose gel electrophoresis and inserted into plasmid pAM1HIJ digested with KpnI and HindIII, generating plasmid pAM1HIJKLMN. Plasmid pAM1HIJKLMN was digested with BamHI and HindIII and the insert was purified by agarose gel electrophoresis and inserted into plasmid pAM1ABCDEFG digested with BamHI and HindIII, generating plasmid pAM1-1. These cloning steps are depicted in Figures 6A-6E ~~Figure 6.~~ Figures 7A-7C ~~Figure 7~~ show the DNA sequence of the insert contained in pAM1-1 (SEQ ID NO:1). This insert can be cloned into any suitable expression vector as a NheI-SmaI fragment to generate an expression construct. pXF8.61 (Fig. 4), pXF8.38 (Fig. 11) and pXF8.224 (Fig. 13) are examples of such a construct.

Please replace the paragraph at page 54, line 30 to page 55, line 10, with the following amended paragraph:

The "LE" version of the B-domain-deleted-FVIII optimized cDNA contained in pAM1-1 was modified by replacing the Leu-Glu dipeptide (2284-2289) at the junction of the heavy and light chains with four Arginine residues, making a total of five consecutive Arginine residues (SEQ ID NO:2). This was achieved as follows. The six oligonucleotides shown in Table 4 were annealed, ligated, digested with EcoRI and HindIII and cloned into pUC18 digested with EcoRI

and HindIII, generating the plasmid pAM8B. Figure 8 shows how these oligonucleotides anneal to form the requisite DNA sequence. pAM8B was digested with BamHI and BstXI and the 230bp insert was purified by agarose gel electrophoresis and used to replace the BamHI(2126)-BstXI(2352) fragment of the "LE" version (See Figures 7A-7C ~~Figure 7~~). Figures 9A-9C ~~Figure 9~~ show the sequence of the resulting cDNA (SEQ ID NO:2). This "5Arg" version of the B-domain-deleted-FVIII optimized cDNA can be cloned into any suitable expression vector as a NheI-SmaI fragment to generate an expression construct. pXF8.186 (Figure 3) is an example of such a construct.